

Intravascular Imaging and Coronary Artery Disease

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TCT-636

Head to head comparison between ultrasound-based virtual histology and real histology in human coronary arteries

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Background: Intravascular ultrasound-derived virtual histology (IVUS-VH) is used to identify VH thin-cap fibroatheromas (with > 10% of NC), which have been demonstrated as predictors of events. Although IVUS-VH has been repeatedly validated, the contrasting results obtained raise some concerns on its accuracy. The aim of this study was to test the correlation between VH and real histology in detecting necrotic core (NC) in ex-vivo human coronary arteries.

Methods: A total of 9 consecutive explanted hearts were included in the study. IVUS-VH analysis was performed immediately after heart collection in a coronary segment clearly identified by metallic needles and thereafter analyzed by real histology. Correlation analysis was performed using linear regression models at cross-section level, with correction for repeated measurements per patient, and at segment level. ROC curves were developed for detection of NC.

Results: Overall, 321 mm were analyzed corresponding to 642 IVUS-VH frames and corresponding histological slices. IVUS-VH and histological NC areas were 0.24 ± 0.43 and 0.16 ± 0.43 mm², respectively. At cross-section level, the correlation between necrotic core size determined by VH and histology was moderate in absolute value ($r=0.50$, $p<0.001$) and poor in relative value ($r=0.43$, $p=0.120$). At the segment level, the NC correlation between VH and RH improves in terms of absolute values ($r=0.80$, $p=0.01$), but was not significant in terms of relative value ($r=0.43$, $p=0.25$). The ROC curves for detection of necrotic core presence and for detection of a threshold of at least 10% NC showed a C-statistics of 0.904 and 0.637, respectively (both $p<0.001$).

Conclusions: Although VH may accurately identify presence of NC, it is not able to accurately quantify the area of NC within the corresponding histological specimen.

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Intravascular Ultrasound and Photoacoustic Imaging of Plasmonic Nanoparticles for Combined Diagnosis and Image-Guided Therapy of Atherosclerotic Plaques

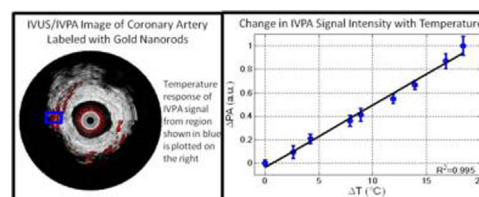
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Background: Recently, intravascular ultrasound (IVUS) guided photoacoustic (IPVA) imaging has been introduced as a means of providing complimentary morphological and compositional assessment of atherosclerotic plaques, including localization of nanoparticle contrast agents within macrophages. Herein, we further demonstrate a method for targeted, locoregional hyperthermia-induced apoptosis of macrophages guided by IVUS/IPVA temperature mapping within plaques.

Methods: Tissue phantoms and ex-vivo coronary artery sections injected with silica-coated gold nanorods were imaged using an integrated IVUS/IPVA imaging catheter comprised of a side looking optical fiber, delivering nanosecond laser pulses for photoacoustic signal generation, coupled to an IVUS transducer. Temperature sensitivity of IVUS/IPVA imaging was verified by first changing the temperature of the surrounding water bath. Subsequently, a continuous wave laser was additionally coupled into the integrated catheter's optical fiber to induce heating of the nanoparticles during IVUS/IPVA imaging.

Results: The measured IPVA signal from the silica gold nanorods was found to vary linearly with temperature, allowing for accurate temperature mapping. Incorporation of the CW laser led to a local temperature rise surrounding the nanoparticles, offering a possibility to induce selective apoptosis of macrophages phagocytically labeled with nanoparticles.

Conclusions: IVUS/IPVA imaging may be utilized as a platform for theranostics of atherosclerosis through imaging of plasmonic nanoparticles with subsequent local temperature monitoring during laser-induced hyperthermia.



TCT-638

Plaque Characteristics and Local Release of C-reactive Protein: An Integrated Backscatter Intravascular Ultrasound Study

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Background: Local release of C-reactive protein (CRP) in human coronary arterial plaque was reported to be greater in acute coronary syndrome than in the stable plaque. Recently, integrated backscatter intravascular ultrasound (IB-IVUS) based tissue characterization has been reported to be useful to detect vulnerable plaque. The purpose of our study was to clarify the relationship between IB-IVUS based plaque characteristics and local high sensitivity (hs-) CRP release in stable and unstable angina pectoris.

Methods: A total of 18 angina pectoris patients (9 stable and 9 unstable angina) were prospectively enrolled. Blood samples proximal and distal to the culprit lesion were obtained via a microcatheter to measure locally produced CRP. Translesional hs-CRP was defined as distal – proximal concentrations of hs-CRP. Gray-scale and IB-IVUS (Terumo, Tokyo, Japan) analysis were performed at the cross section with the smallest lumen cross sectional area (CSA) of target lesion. External elastic membrane (EEM) CSA and lumen CSA were measured and plaque + media (P + M) CSA was calculated as EEM minus lumen CSA. IB-IVUS based plaque characterization was classified as fibrosis, dense fibrosis, calcification and lipid pool. Relationships between translesional hs-CRP gradient and gray scale as well as IB-IVUS indices were investigated.

Results: Systemic hs-CRP level did not correlate significantly with any IVUS parameters. However, P + M CSA and % lipid pool area by IB-IVUS correlated positively and significantly with translesional hs-CRP level (P + M CSA; $p < 0.01$, $r = 0.68$, % lipid pool area; $p = 0.02$, $r = 0.54$).

Conclusions: Local release of CRP is related to size of the lipid pool. IB-IVUS based tissue characterization may be useful in detecting local inflammation suggestive of plaque vulnerability.

TCT-639

NR4A3 as a gene expression marker of acute atherosclerotic plaque rupture in STEMI

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Background: Circulating endothelial cells (CECs) that line the coronary artery endothelium are sloughed off during atherosclerotic plaque rupture preceding myocardial infarction (MI). Comparison of gene expression levels in these cells between those experiencing an MI and healthy controls may determine the genes associated with the deleterious CECs released during coronary artery atherosclerotic plaque rupture.

Methods: Blood was collected from 21 MI patients and 22 age-matched healthy donors. CECs were isolated using the CellSearch system with the CellSearch CEC Profile kit. The total RNAs were isolated from CECs according to standard Trizol method. Following hybridization, arrays are washed and stained before scanning on the Affymetrix GeneChip. Using the first 12 myocardial infarction subjects and 13 healthy age matched controls a database containing a training collection of approximately 54,000 expression patterns was created. Principal components analyses of CEC gene expression profiles were used to discriminate myocardial infarction subjects from healthy controls. Estimation of classification performance was then carried out in an independent set of 9 myocardial infarction patients and 9 healthy controls. The highest-ranking genes by means of AUC classification performance were ranked after controlling for stable atherosclerotic disease, inflammatory conditions and CEC count.

Results: Principal component 1 accurately classified an independent collection of 9 MI's and 9 healthy controls. The area under the receiver-operating characteristic (ROC) curve for the classifier developed from the PCI analysis was 0.9. After controlling for comorbid disease states and normalizing the gene set for CEC count the gene NR4A3 was the highest-ranking gene with an AUC classification performance of 0.98 in the training set and 0.94 in the test set.

Conclusions: Gene expression profiles isolated from CECs accurately discriminate MI patients from healthy controls. This molecular signature may be useful for developing an assay for identifying atherosclerotic plaque rupture preceding myocardial infarction. NR4A3 was the highest-ranking gene by virtue of AUC classification performance of MIs and controls.